AMENDMENTS TO THE DRAWINGS

Please replace Fig. 22B with the Replacement Sheet for Fig. 22B.

REMARKS

1. Formal Matters

a. Status of the Claims

Claims 31-42 are pending in the instant application. Claims 37-38 are hereby canceled without prejudice to pursuing the canceled subject matter in a continuing application; and claims 31-36 are amended. Upon entry of these amendments, claims 31-36 and 39-42 are pending and under active consideration. Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the instant application.

b. Amendments to the Claims

Claim 31 is amended to recite, "An isolated nucleic acid consisting of X nucleotides," wherein X=19 to 140, which a rephrasing of the recitation, "An isolated nucleic acid consisting of 19 to 140 nucleotides." Claim 31, limitation (a) is amended to recite "Y consecutive nucleotides of SEQ ID NO: 6527," wherein Y≥19 and X≥Y, which is a rephrasing of the recitation, "at least 19 consecutive nucleotides of SEQ ID NO: 6527." These amendments do not change the scope of the claim.

Claim 31, limitation (b) is amended to recite "a DNA equivalent of (a)," support for which can be found at paragraph 0044 of the specification as originally filed. Paragraph 0044 in part recites, "A Nucleic acid is defined as a ribonucleic acid (RNA) molecule, or a deoxyribonucleic acid (DNA) molecule…"

Claim 31, limitation (c) has been stricken so that claim 31 no longer recites "a sequence at least 80% identical to (a) or (b)." Accordingly, claim 31, limitation (d) is now limitation (c), and is amended to recite "the complement of (a) or (b).

Claim 32 is amended recite, "The nucleic acid of claim 31, wherein the Y nucleotides…," which is a rephrasing of the recitation, "The nucleic acid of claim 31, wherein the at least 19 nucleotides," and antecedent basis for which can be found at amended claim 31. This amendment does not change the scope of the claim. Claim 32 is also amended to correct a typographical error.

Claim 33 is amended to recite, "The nucleic acid of claim 31, wherein X=19 to 24 nucleotides," which is a rephrasing of the recitation, "The nucleic acid of claim 31, wherein the nucleic acid consists of 19 to 24 nucleotides," and antecedent basis for which can be found at amended claim 31. This amendment does not change the scope of the claim.

Claim 34, limitation (a) is amended to recite, "The nucleic acid of claim 31, wherein X=Y," antecedent basis for which can be found at amended claim 31. This amendment does not change the scope of the claim.

Claim 35 is amended to recite, "The nucleic acid of claim 32, wherein X=Y," support and antecedent basis for which can be found at amended claims 31 and 32.

Claim 36 is amended to recite, "The nucleic acid of claim 33, wherein X=Y," support and antecedent basis for which can be found at amended claims 31 and 33.

c. Amendments to the Specification

Paragraph 0110 and 0112 are amended to assign the appropriate SEQ ID NOs to the sequences shown in Figures 23B and 24A in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0032 is amended to incorporate the Sequence Listing submitted herewith by reference.

d. Amendments to the Drawings

Figure 22B is replaced with the Replacement Sheet for Fig. 22B to assign the appropriate SEQ ID NOs to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

2. Preliminary Remarks

a. Sequence Rule Compliance

On pages 3 and 4 of the Office Action, the Examiner alleges that the instant application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. The Examiner has requested that Applicant amend either the drawings or the Brief Description of the Drawings in the specification to assign each sequence a corresponding SEQ ID NO. Paragraphs 0110 and 0012 of the Brief Description of the Drawings, and Fig. 22B are amended herein to assign SEQ ID NOs to the sequences shown in Figs. 22B, 23B and 24A. Accordingly, Applicant submits that the instant specification complies with 37 C.F.R. §§ 1.821-1.825 and respectfully requests that the Examiner reconsider and withdraw the objection to the application for lack of sequence rule compliance.

b. Claim Objections Under 37 C.F.R. § 1.75(c) - Claims 34, 36, 37, 38, 40, and 42

On page 6 of the Office Action, the Examiner objects to claim 34, 36, 37, 38, 40, and 42 under 37 C.F.R. § 1.75(c) for allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claims 37 and 38

The Examiner asserts that the phrase, "wherein the nucleic acid is an RNA" of claims 37 and 38, does not further limit the scope of the subject matter of claims 32 and 35. Claims 37 and 38 are canceled without prejudice, thereby rendering the objection to these claims moot.

Claim 34

The Examiner asserts that use of the transitional phrase "consists of" in claim 34, which depends from claim 35, does not further limit the scope of claim 35. Applicant respectfully disagrees. However, in order to expedite prosecution of the instant application, claim 31 is amended to recite a nucleic acid of X nucleotides, wherein X=19 to 140, and wherein the sequence of the nucleic acid comprises at least Y consecutive nucleotides of SEQ ID NO: 6527, wherein Y≥19 and X≥Y. Accordingly, the nucleic acid of claim 31 may include 19 or more consecutive nucleotides of SEQ ID NO: 6527, as well as additional nucleotides. For example, the nucleic acid may include 19 consecutive nucleotides of SEQ ID NO: 6527 and 121 other nucleotides.

Claim 34 is amended to recite, "The nucleic acid of claim 31, wherein X=Y." Accordingly, the nucleic acid of claim 34 consists only of at least 19 consecutive nucleotides of SEQ ID NO: 6527. Using the above example for claim 31 of the nucleic acid including 19 consecutive nucleotides of SEQ ID NO: 6527 and 121 other nucleotides, the nucleic acid of claim 34 depending from this sequence would consist of 19 consecutive nucleotides of SEQ ID NO: 6527. Applicant respectfully submits that amended claim 34 properly further limits the scope of amended claim 31.

Claims 36, 40, and 42

The Examiner objects to claims 36, 40, and 42 due to their dependency on claim 34. Applicant respectfully submits that amended claim 34 is in proper dependent form. Accordingly, Applicant respectfully submits that claims 40 and 42 are proper. Applicant notes that amended claim 36 now depends from claim 33, not claim 34.

In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the objection to claims 34, 36, 37, 38, 40, and 42 under 37 C.F.R. § 1.75(c).

3. Patentability Remarks

a. 35 U.S.C. § 112, Second Paragraph

Claims 31-42, "RNA equivalent"

On pages 7-9 of the Office Action, the Examiner rejects claims 31-42 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner asserts that the scope and precise meaning of the term "RNA equivalent" of claims 31 and 34 is unclear, rendering the true breadth of the claims as a whole unclear. Applicant respectfully disagrees. However, in order to expedite prosecution of the instant application, claims 31 and 34 are amended to no longer recite the term "RNA equivalent," thereby rendering the rejection moot. The Examiner rejects claims 32, 33, and 35-42 due to their dependence on

claim 31 or 34. In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 31-42 under 35 U.S.C. § 112, second paragraph.

Claims 32, 35, 37, and 38, "wherein the at least 19 nucleotides comprises the sequence of SEQ ID NO: 15"

On page 9 of the Office Action, the Examiner rejects claims 32, 35, 37, and 38 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Specifically, the Examiner asserts that the term "wherein the at least 19 nucleotides comprise the sequence of SEQ ID NO: 15" in claims 32 and 35, is indefinite because SEQ ID NO: 15 is a 22-mer, and it is unclear how a 19-, 20-, or 21-mer may comprise a 22-mer. Applicant respectfully disagrees. Applicant submits that the essential inquiry is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. *See* M.P.E.P. 2173.02. Applicant further submits that a claim must be considered as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope, and provides clear warning to others as to what constitutes infringement of the patent. *Id.*

Applicant respectfully notes that amended claim 31 in part recites "Y consecutive nucleotides of SEQ ID NO: 6527," wherein Y≥19, and that amended claim 32 in part recites, "The nucleic acid of claim 31, wherein the Y nucleotides comprise the sequence of SEQ ID NO: 15." Applicant respectfully submits that one of ordinary skill in the art would recognize that the nucleic acid of claim 31 may comprise as few as 19 consecutive nucleotides of SEQ ID NO: 6527 (*i.e.*, Y=19). Applicant further submits that one of ordinary skill in the art would also recognize if the nucleic acid of claim 31 comprises the sequence of SEQ ID NO: 15 (*i.e.*, the Y nucleotides comprise the sequence of SEQ ID NO: 15; the subject matter of claim 32), then the nucleic acid must be at least 22 nucleotides in length, and can not possibly be 19, 20, or 21 nucleotides in length. Accordingly, Applicant respectfully submits that claim 32 sets out and circumscribes a particular subject matter with a reasonable degree of clarity and particularity to one of ordinary skill in the art.

Applicant respectfully notes that amended claim 35 is related to a nucleic acid consisting of the sequence of SEQ ID NO: 15 and must therefore be 22 nucleotides in length. Applicant also notes that claims 37 and 38 are canceled without prejudice, thereby rendering the rejection of these claims moot.

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 32, 35, 37 and 38 under 35 U.S.C. § 112, second paragraph.

b. 35 U.S.C. §§ 101 and 112, first paragraph

On pages 6-13, the Examiner rejects claims 14-29 under 35 U.S.C. § 101, for allegedly lacking utility. In order to satisfy the utility requirement under the Revised Interim Utility Guidelines, a specific and substantial utility must either (i) be cited in the specification or (ii) be recognized as well as established in the art, and the utility must be credible.

(1) Specific Utility

A specific utility is defined in the Revised Interim Utility Guideline Training Materials ("RIUGTM") as a utility that is specific to the particular claimed subject matter, which is in contrast to a general utility that would be applicable to a broad class of the invention. For example, a claim to a polynucleotide of which use is disclosed simply as a "gene probe" or "chromosome marker" is not considered to be specific in the absence of a disclosure of a specific DNA target. *See* RIUGTM at page 5.

At page 16 of the Office Action, the Examiner alleges the specification does not disclose any specific function of the claimed nucleic acids aside from indicating it may be expressed in certain cells or present in certain genomes. The Examiner further asserts that the Applicant fails to identify whether abnormal expression of the claimed nucleic acids is casually related to any disease or condition. The Examiner concludes that the only recognizable utility of the claimed nucleic acids is diagnostic probes for scientific research. Applicant respectfully disagrees. The application discloses that the claimed nucleic acids may be used to regulate expression of specific genes of interest.

For example, at paragraphs 63-69 of the specification, it is asserted that the disclosed polynucleotides may be used to target and modulate expression of particular host target gene transcripts *in vivo* or *in vitro*. Furthermore, the specification discloses that the claimed polynucleotides, which are related to miRNAs encoded by the GAM1032 gene, modulate expression by inhibiting translation of the target mRNA transcript Choline Acetyltransferase (ChAT) as shown in Table 7, lines 1468-1501, and Table 8, lines 7124-7275. Accordingly, Applicant submits a specific utility is provided by the specification with regard to studying the modulation of expression of the ChAT gene.

(2) Substantial Utility

A substantial utility is defined in the RIUGTM as a utility that defines a "real world" use, which is in contrast to the need to carry out further research to identify or confirm a "real world" context.

At page 12 of the Office Action, the Examiner asserts that the utility of regulating ChAT by the claimed polynucleotides in Table 8 is not substantial because there is no disclosure establishing a nexus between the claimed nucleic acid sequences SEQ ID NOs: 6527 and 15 and the treatment, diagnosis or identification of any disease or disorder. In addition, the Examiner alleges that the Applicant has failed to

provide a teaching that the only recognizable utility is a diagnostic probe with no practical purpose beyond methods of gene expression analysis. Applicant respectfully disagrees.

As discussed above, the claimed polynucleotides may be used to regulate expression of proteins encoded by the human host gene ChAT. Lines 3133-3128, Table 8 disclose that the gene ChAT encodes the neurotransmitter acetylcholine and is therefore associated with Alzheimers. Table 8 also discloses that ChAT is directly implicated with congenital myasthenic syndrome associated with fatal episodes of apnea. Ohno *et al., PNAS* 98:2017-2022 (2001), which is submitted on the Information Disclosure Statement filed herewith, discloses that mutations of the gene ChAT is known to be associated with congenital myasthenic syndrome. Applicant submits that one of ordinary skill in the art would recognize that the claimed polynucleotides may be used to regulate expression (*in vitro* or *in vivo*) of a gene such as ChAT and thereby study the role of this target gene's associated diseases such as Alzheimers and congenital myasthenic syndrome. Accordingly, Applicant respectfully submits that the specification provides a substantial utility for the claimed polynucleotides.

(3) Credible Utility

According to the RIUGTM, an asserted utility is credible if the assertion is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided. An assertion is credible unless (i) the logic underlying the assertion is seriously flawed, or (ii) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. *See* RIUGTM at page 5.

At page 14 of the Office Action, the Examiner asserts that a credible utility is lacking because the claimed nucleic acids have not been shown to even be expressed, or if expressed artificially target and inhibit a particular gene in order to be used to prevent, treat, or diagnose a disease or condition. Applicant respectfully disagrees.

Applicant respectfully submits that that specification does not simply provide "throw away" utilities for the claimed nucleic acids. Rather, the Applicant submits that the Examiner has not considered the asserted utility as discussed above for using the claimed polynucleotides for modulating expression of specific mRNA targets. Whether or not the claimed polynucleotides actually exist or are expressed in a biological system, and whether the true biological function of any predicted miRNA sequence has been validated according to Krutzfeldt (cited by Examiner on pages 9 and 10 of the Office Action) **are irrelevant**. The proper inquiry is instead whether a person of ordinary skill in the art would believe that the claimed polynucleotides **may be** used to modulate expression of the specific mRNA targets.

Paragraph 181 of the application discloses that the mRNA targets of the claimed nucleic acids were identified as being consistent with the free energy and spatial structure of target binding sites of

known miRNAs. The method as described in paragraphs 235-255 for identifying target binding sites of miRNAs demonstrates that miRNAs bind to target binding sites. In view of the asserted utilities being consistent with the general understanding of miRNAs and their target binding sites at the time of filing, Applicant respectfully submits that one of ordinary skill in the art would believe that each claimed polynucleotide would bind its respective target binding sites.

In view of the foregoing remarks and lack of showing that Applicant's assertion of utility is seriously flawed or logically inconsistent, the Applicant respectfully submits that a credible utility is asserted for the claimed polynucleotides.

c. 35 U.S.C. § 112, first paragraph

On page 18 of the Office Action, the Examiner rejects claims 31-42 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner asserts that because the claimed subject matter is not supported by either a specific, substantial, and credible asserted utility or a well established utility as the Examiner asserts above, one skilled in the art clearly would not know how to use the claimed subject matter.

Applicant respectfully submits that, as described above, the claimed subject matter has a specific, substantial, and credible asserted utility, as well as an established utility. As discussed above, claims 37 and 38 are canceled without prejudice. In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 31-42 under 35 U.S.C. § 112, first paragraph.

d. 35 U.S.C. § 102

On pages 18-20 of the Office Action, the Examiner rejects claims 31, 33, 34, 36, and 39-42 under 35 U.S.C. § 102(e) as allegedly being anticipated by Tuschl *et al.* (U.S. Pat. App. Pub. No. 2005/0059005; "Tuschl" hereafter). The Examiner asserts that Tuschl discloses two separate 22-nucleotide RNAs that are at least 80% identical to the nucleic acids recited in amended claim 31. Amended claim 31 is related to "An isolated nucleic acid consisting of X nucleotides wherein the sequence of the nucleic acid comprises: (a) Y consecutive nucleotides of SEQ ID NO: 6527; (b) a DNA equivalent of (a); or the complement of (a) or (b), wherein, X=19 to 140, Y≥19, and X≥Y." Applicant submits that Tuschl does not teach the nucleic acid of claim 31. Claims 33, 34, 36, and 39-42 draw their dependency from claim 31. Accordingly, Tuschl does not teach all the limitations of claim 31 or its dependents. In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 31, 33, 34, 36, and 39-42 under 35 U.S.C. § 102(e).

4. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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Dated: July 2, 2007

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